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Case Report

Prenatal onset of sporadic form of infantile cortical hyperostosis

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ABSTRACT

Infantile cortical hyperostosis, Caffey's disease, is characterized by cortical swelling of one or several flat or long bones, fever, irritability and decreased movement of the affected bones. The onset of presentation is around ten weeks of age, however, antenatal cases with familial and sporadic forms have being reported. The etiology is unknown. Autosomal dominant or recessive inheritance and sporadic cases have been reported. Present case report describes a mild, antenatal and sporadic form of Caffey's disease in a newborn infant, who presented with painless swelling and deformity of the right tibia and right forearm.

Keywords: Caffey's disease, New-born

INTRODUCTION

Infantile cortical hyperostosis (ICH) is a rare proliferative disease affecting infants, with age of onset around ten weeks of age and usually manifests within the first 7 months of life, although there have been cases reported appearing much later in childhood.

It is usually a self- limiting disease characterized by irritability, fever, and development of bowing, usually tender, non-hyperemic, non-suppurative swelling over one or more bones. Radiological examination shows swelling of the diaphyseal cortex of the affected bones. Initially, irregular cortical thickenings which later may become laminated as healing occurs.[1,2]

Two forms of Caffey's disease have been recognized; a prenatal presenting in utero or at birth and could be mild or severe and the classical form which is mild and presents within the first 6 months of live.

The severe form is characterized by onset before 35 weeks gestation, polyhydramnios, hydrops fetales, hypoplastic lungs, prematurity and extensive hyperostotic bone involvement; it has a poor prognosis with almost 100% lethality.[3,4] The manifestations of the mild prenatal form are not detected before 35 weeks gestation and there is less incidence of polyhydramnios and bone involvement.[5]

The etiology is unclear; both the prenatal and classical form could be familiar or sporadic. The familial form could be inherited as autosomal dominant with incomplete penetrance. A phenotype of Caffey's disease, secondary to viral, immunologic, and environmental influences could exist explaining the recognition of sporadic cases.[6,7] Present case report describes a mild sporadic prenatal form of ICH, which presented at birth with involvement of tibia, fibula and ulna in an asymptomatic infant.

CASE REPORT

A female infant was born by normal spontaneous vaginal delivery (NSVD) to a 29-year-old gravida 2, Para 1, Hispanic mother who had an uneventful pregnancy, all

prenatal laboratory and sonogram findings were within normal limits. The Apgars were 9 and 9 at 1 and 5 minutes; birth weight was 3175 gm, head circumference 33 cm, length of 49 cm, which were all at the 50th percentile for her gestational age. The infant was afebrile with normal vital signs. The baby presented at birth with painless swelling of the right lower leg (Figure 1), and forearm, rest of the physical examination was unremarkable.

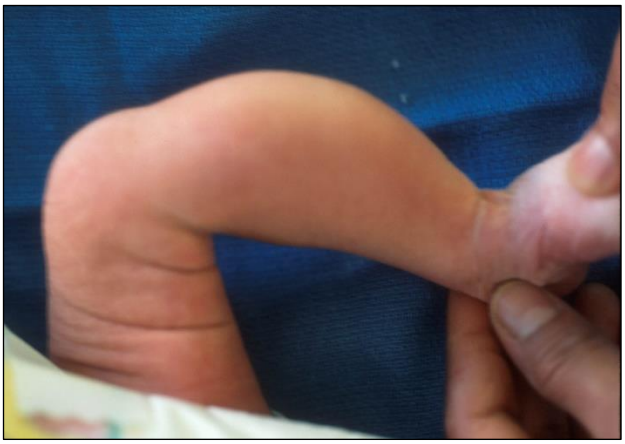

Figure 1: Bowing of right lower leg.

Laboratory studies disclosed a hemoglobin of 15.8 g/dl, leukocyte count 13,200/mm^3 with a differential of 30% lymphocytes, 58% neutrophils, and erythrocyte sedimentation rate of 11 mm/hr. Serum calcium of 10.8 mg/dl, alkaline phosphatase 653 U/L, and vitamin A levels 27 units (WNL). Blood, CSF and urine bacteria cultures were all negative. Urine for CMV was reported negative, toxoplasma IGG - 41.5 IU/ml, IGM - 0.05 IU/ml, RPR was non-reactive. Radiological examination revealed marked bowing and bony sclerosis of the right tibia, fibula and both ulnas (Figure 2).

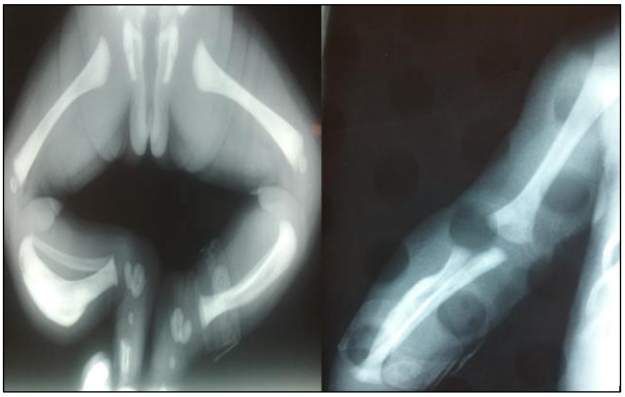

Figure 2: Bowing and hyperostosis of the tibia and ulna presented at birth.

Skin biopsy revealed that the type I and III procollagen and collagen as examined by protein gel electrophoresis were normal, thereby ruling out Osteogenesis Imperfecta. A non-contrast head CT scan was found to be normal. No history of ICH nor a family history of any skeletal dysplasia could be elicited from the parents or extended families. A diagnosis of the sporadic form of congenital infantile hyperostosis was made. No drug treatment was instituted, and the child was discharged with routine newborn care follow up. The infant at 15 months of age had a weight, height and head circumference with appropriate growth at the 50 percentile, completely asymptomatic and developmentally age appropriate. The bone lesions in the upper extremities have resolved and the angulation of the right tibia has decreased from a 70-degree angle to a 35-degree angle.

DISCUSSION

The case reported here is an antenatal onset of a mild form of ICH. Literature indicates that mild sporadic antenatal form of the disease is less common than familial forms.

The genetic etiology of the disease is heterogeneous; various studies have supported the finding that a mutation in the type I collagen alpha1 chain gene (COL1A1) is responsible for this disease.[7,8] Some have suggested that transmission may occur via an infectious agent with a long latency period. Other theories have included a primary arterial abnormality and allergic reaction. It is possible that the gene responsible for the condition varies in expressivity, with some cases being mild which may be missed without radiological examination whereas in others the disease may have a prolonged and severe course.[9-11]

In Caffey's disease usually, there are no radiographic evidence of destruction or interruption of cortex and all blood cultures remain negative. There are few reported cases of lytic bone lesions, but those are very rare.[12]

The differential diagnosis of ICH includes hypervitaminosis A, syphilis, post-traumatic bone changes (battered baby syndrome), osteogenesis imperfecta, osteomyelitis and long-term prostaglandin E therapy.[13,14]

Children with a daily vitamin A, intake of 1500 IU/kg body weight of several months duration are at risk for toxicity.[15] Hypervitaminosis A results in skeletal abnormalities such as cortical thickening of the tubular bones, cupping and fraying of the metaphyses, irregularity of the growth plates, and premature fusion of the ossification centers. These effects are distinguished from Caffey's disease by the absence of mandibular involvement, higher probability of metaphyseal involvement, lack of fever, and occurrence after 4 months of age.[16]

In congenital syphilis the bone involvement tends to be multiple, symmetrical and include osteochondritis,

osteomyelitis and periostitis. These radiographic signs are accompanied by positive serology.[17]

Battery baby syndrome is differentiated from Caffey's disease by the presence of multiple fractures at different stages of healing, delay in obtaining medical treatment, and the presence of other organ injuries.[18]

Osteogenesis imperfecta (OI), a genetic disorder of collagen synthesis, is characterized by bones that break easily from little or no apparent cause. Radiographic findings include osteoporosis of both the axial and appendicular skeleton, over tubulation (gracile) of long bones, and healing fractures.[19]

Most cases of OI are autosome dominant, with less than 50% of cases represented by new mutations. The diagnosis is confirmed by collagen biochemical studies or sequence of cDNA using fibroblasts cultured from skin punch biopsy or by direct sequencing of DNA from leukocytes.

In osteomyelitis the X ray findings can overlap with Caffey's disease, typical early bony changes include: periosteal thickening, lytic lesions, endosteal scalloping, osteopenia, loss of trabecular architecture, and new bone apposition.[20]

Clinical manifestations in neonates include pseudoparalysis or pain with movement of the affected extremity, edema, erythema and warm at the site.[21]

Cortical hyperostosis has been identified in cases of lengthy periods of prostaglandins use; usually after prostaglandin therapy of 40 days' duration or more, although it also has been demonstrated as early as 9 days after the initiation of therapy. The mechanism by which prostaglandin E causes periosteal new bone appears to be related to its physiologic role as an inflammatory mediator. Symmetric involvement of long bones ribs, clavicles, and scapulae is typical; rarely, the mandible may be affected.[22]

Most cases of ICH resolved by three years of age, radiological findings may be seen up to 11 months after disappearance of apparent swelling of bones. Treatment is supportive.

Other laboratory findings, include elevation of sedimentation rate, serum alkaline phosphates, and white blood cell count with lymphocytosis, mild anemia.

CONCLUSION

This case described an atypical sporadic form of an extremely rare disorder, presenting at birth with painless involvement of long bones in a new-born infant. Neonatologist who deal with infants presenting with such bony deformities at birth should be aware of the still prevalent sporadic form of ICH, which usually is self-limiting with good prognosis, thus alleviating the anxiety experienced by the parents of the affected infant.

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